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Increased DKA and Hyperglycemia During a COVID 19 Surge, a Retrospective Observation.

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***Patient**: Multiple, Retrospective Review of cases over a period of 1 month in the Middle of a COVID 19 Surge.*

***Final Diagnoses:** DKA, COVID-19, Diabetes, Hypoxic Respiratory Failure*

***MeSH Keywords:** DKA, COVID-19, Diabetes, Hypoxic Respiratory Failure, Glycemic Control, Hyperosmolar Hyperglycemia State*

***Objective:** Unusual clinical course*

Abstract

During the middle of a COVID-19 surge a retrospective review of cases in a COVID ICU was performed over a one month of surge. All patients had COVID-19 confirmed by PCR testing and had a degree of respiratory insufficiency ranging from hypoxemia corrected with a minimum of 2 liters of oxygen by nasal cannula up to 100 percent oxygen with mechanical ventilation. They all had lung protective strategies and mechanical proning. We saw an average of 20 percent of our patient population having active DKA and a significant increase in hyperglycemia in the rest of the patients. These findings are consistent with similar observations seen in multiple ICUs in America and the world. Increased morbidity and mortality have been reported in these patients, indicating prompt attention in correcting fluid status, insulin supplementation and electrolyte imbalances as a priority by the intensive care team. Furthermore, all COVID patients receiving steroids as part of the anti-inflammatory therapy should be monitored for abnormal or worsening blood sugars.

Background

Diabetes has been associated as a major risk factor in developing complications with severe SARS-CoV-2 infection. Most of these patients have DM type 2. Over the past year there has been an increase in type 2 diabetics presenting with diabetic ketoacidosis (DKA). Several adult patients with Diabetes Mellitus have presented with COVID related DKA

DKA is the most common hyperglycemic emergency in the ICU seen in the middle of the surge with Omicron, Delta and with previous COVID strain surges in America. We have seen an increase in diabetic patients presenting concomitant infection with SARS-CoV-2. The US has surpassed 990,000 fatalities, with over 80 million cases in America.

There has been an increase in numbers of type 1 and 2 diabetic patients with COVID-19. These patients have an increased rate of morality compared to non-COVID-19 patients. Traditional viral infections have increased the likelihood of the destruction of β-cells in people with underlying genetic risk for diabetes. The unregulated immune response as the virus attaches to the ACE 2 receptors can also cause direct destruction of the pancreatic βeta cells. SARS-CoV-2 can cause direct destruction of β-cell in the pancreas causing hyperglycemia as further damage of endogenous insulin is exacerbated by direct viral infection. This can fuel a more robust proinflammatory cytokine response, increase in C reactive protein and pro inflammatory cytokines IL-6 that have been associated with an increased mortality.

Prior to the pandemic, the most common risk factors for admitting DKA patients to the ICUs had been low socioeconomic status, younger age, female patients, and elevated hemoglobin A1C. It is possible that social isolation itself, self-quarantine and poor access to care or medication can also be contributing factors to increases in DKA during the pandemic. Prior to COVID, America already had an epidemic of obesity with over 40 percent of its citizens being obese and more than 10 percent of the citizens, over 34 million being diabetic. As Delta, Omicron and other strains propagated and exerted direct damage to the pancreatic cells causing further decreased insulin production and promoting inflammation. DKA patients have a higher risk and mortality in our hospitals, and ICUs. The large body habitus, large frame and increased BMI have worse outcomes and can succumb to multiorgan dysfunction.

Methods

A retrospective review of cases during one month in the middle of the pandemic was performed. We had full capacity of 25 ICU beds. At any one point we had over 20 patients with a blood sugar > 275 mg /dl, average admission of 4-5 new COVID patients per day. I personally rounded on all of them. Blood Glucose level > 360. Bicarbonate level less than 19. Anion Gap > 12 on all of them pH less than 7.25 on all of them. Positive ketonemia or ketonuria. All the patients had the above-mentioned parameters. These figures represent about 20 percent of all COVID patients seen any day during the week. All patients had hypoxic respiratory failure requiring supplemental oxygen, high flow or mechanical ventilation. All patients without DKA had blood sugars of > 200.

Results

There was a 20 percent of patient increased in DKA patients in the middle of this surge in our ICU. These patients had SARS-CoV-2. All had BMI > 30, 75 percent Caucasian and 25 percent Afro-American, 40 percent of the patients had BMI of 35 percent. All patients were hypoxic, all had ground glass opacities, all were treated with Remdesivir, steroids and antibiotics. All required oxygen supplementation from 28 percent oxygen to 100 percent on the ventilator. All of them had protracted hospitalizations, and despite the complex management of this group, they all survived, and all were in the acute hospital

for more than 2 weeks. The main limiting factor for discharge was their high oxygen requirements. All had abnormal HgA1c and were diabetic. Of these patients, 85 percent were not vaccinated, only three had been vaccinated. Of these, 2 had been treated with chemotherapy for lung cancer and 1 with Rituximab for systemic lupus erythematosus (SLE). The average age for this cohort was 48.15 years.

Parameter	Age	BMI	Initial Random blood sugar	HgA1c	WBC	Bicarbonate	AG	Ventilator	percent of oxygen requirement	Vaccinated
Patient 1	34	32	745	9.8	7234	17	14	yes	100%	no
Patient 2	42	35	670	8.1	8900	15	23	yes	100%	no
Patient 3	38	42	543	110	1100	13	21	no	100%	no
Patient 4	56	37	500	12.2	1300	11	16	no	90%	no
Patient 5	54	35	427	8.9	7100	14	25	no	75%	no
Patient 6	54	37	678	11.2	9230	13	23	yes	80%	yes
Patient 7	45	45	876	7.5	1100	19	21	yes	90%	no
Patient 8	38	33	672	9.8	1200	17	17	yes	80%	no
Patient 9	39	36	350	12.3	7899	15	16	no	75%	no
Patient 10	59	36	467	11.3	7200	13	18	no	100%	yes
Patient 11	67	37	765	9.9	7100	15	24	no	80%	yes
Patient 12	62	38	525	12.2	8200	18	22	yes	90%	no
Patient 13	71	37	513	11.1	8100	15	21	yes	100%	no
Patient 14	45	33	780	9.4	8200	13	16	yes	95%	no
Patient 15	48	37	673	9.8	7500	12	22	yes	90%	no
Patient 16	42	35	356	9.7	7800	15	21	yes	70%	no
Patient 17	38	39	434	9.8	8900	16	22	yes	80%	no
Patient 18	38	38	534	9.7	9200	17	25	yes	90%	no
Patient 19	43	38	567	9.5	9100	13	22	no	75%	no
Patient 20	50	37	672	11.1	8600	12	14	no	80%	no
Average	48.15	36.9	587.35	15.165	6748.15	14.65	20.15	yes	87%	no

Snapshot, over a Month in an ICU during the COVID 19 Pandemic

Discussion

The observation of this retrospective series reveals many diabetes patients with DKA were admitted during the middle of a surge of both Delta and Omicron strains in a COVID ICU. All these patients had increased BMI > 35 and all presented hypoxemia. They were all treated with Remdesivir, steroids, fluids, and antibiotics. All had prolonged hospital admissions of greater than 2 weeks. Eighty fiver percent (17) of these patients were not vaccinated and fifteen percent (3) had vaccines. Out of the three that had vaccines, two had underlying malignancy and one was treated with Anti-CD20, Rituximab for SLE. 75 percent were Caucasian, while 25 percent Afro-American. All had elevated random blood sugars > 350 as well as abnormal HgA1c.

This data set shows a high number of patients were not vaccinated and it suggests that malignancy or autoimmunity is also a strong comorbidity for COVID-19 patients in the ICU. All patients received fluids and standard insulin replacement to close the anion gap. They were all able to leave the ICU and continue their medical care on a COVID medical unit.

Conclusion

DKA and Diabetes has been reported in the world literature to be more prevalent during the pandemic. BMI seems to be the highest risk factor. Abnormal blood sugars are also associated with a high mortality. Any viral infection or secondary infection promotes the pro inflammatory cascade. This increased hyperglycemia, and the direct viral destruction of βeta cells in the pancreas further exacerbate and compound the hyperglycemic effect. Hydration is necessary with insulin supplementation and replacement. Most of these patients presented with morbid obesity, representing an independent risk factor of mortality which is compounded by diabetes. Evaluation for end organ damage due to chronic hyperglycemia is recommended. The use of serial labs, re-expansion of intravascular volume with the adjusted insulin infusion is needed to close the anion gap and subsequently stop glycolysis. The need for follow up care with endocrinology or primary physicians is necessary and diabetic education should be performed on all patients upon discharge from the ICU.

There appears to be a higher incidence of hyperglycemia associated with ketosis in COVID-19 septic patients. It is unknown if this ketosis is associated with sepsis related syndrome versus diabetic related β-cell destruction. There is also no long-term data yet on post COVID recovered patients showing increased insulin requirements. There is a need for further evaluation if insulin deficiency long term is a related effect of post COVID-19 survival. Another key question to be further evaluated is to see if acute COVID-19 infections will create long term sub-acute diabetes versus long term increased insulin requirements for diabetics.

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